MAJOR ARTICLE

Prevalence and Risk Factors for Asymptomatic *Clostridium difficile* Carriage

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Background. *Clostridium difficile* infection (CDI) incidence has increased dramatically over the last decade. Recent studies suggest that asymptomatic carriers may be an important reservoir of *C. difficile* in healthcare settings. We sought to identify the prevalence and risk factors for asymptomatic *C. difficile* carriage on admission to the hospital.

Methods. Patients admitted to Barnes-Jewish Hospital without diarrhea were enrolled from June 2010 through October 2011. Demographic information and healthcare and medication exposures 90 days prior to admission were collected. Stool specimens or rectal swabs were collected within 48 hours of admission and stored at −30°C until cultured. *Clostridium difficile* isolates were typed and compared with isolates from patients with CDI.

Results. A stool/swab specimen was obtained for 259 enrolled subjects on admission. Two hundred four (79%) were not colonized, 40 (15%) had toxigenic *C. difficile* (TCD), and 15 (6%) had nontoxigenic *C. difficile*. There were no differences between TCD-colonized and -uncolonized subjects for age (mean, 56 vs 58 years; $P = .46$), comorbidities, admission from another healthcare facility (33% vs 24%; $P = .23$), or recent hospitalization (50% vs 50%; $P = .43$). There were no differences in antimicrobial exposures in the 90 days prior to admission (55% vs 56%; $P = .91$). Asymptomatic carriers were colonized with strains similar to strains from patients with CDI, but the relative proportions were different.

Conclusions. There was a high prevalence of TCD colonization on admission. In contrast to past studies, TCD colonization was not associated with recent antimicrobial or healthcare exposures. Additional investigation is needed to determine the role of asymptomatic TCD carriers on hospital-onset CDI incidence.

Keywords. *Clostridium difficile* colonization; prevalence; asymptomatic carrier; risk factors.

Increases in the incidence and severity of *Clostridium difficile* infection (CDI) throughout North America and Europe over the past decade have been well described [1–3]. Moreover, recent reports from multiple community hospitals in the United States indicate that *C. difficile* has surpassed methicillin-resistant *Staphylococcus aureus* as the most common cause of healthcare-associated infection [4]. It is estimated that in 2008, CDI may have resulted in excess healthcare costs of $4.8 billion in the United States, and CDI causes >14 000 deaths per year [5, 6].

These changes in CDI incidence and severity have brought renewed attention to CDI prevention. Current prevention efforts focus on preventing *C. difficile* transmission from patients with symptomatic CDI [7, 8]. Unfortunately, the data to support many of the recommendations are weak [9]. Only 2 of 16 recommendations to prevent CDI in acute care hospitals have a strength of "A," or good evidence, to support the recommendation. In addition, many of the recommended prevention practices appear to have a lesser impact on CDI incidence in endemic settings than in epidemic settings [9, 10].

Prevention efforts have focused on preventing transmission from patients with CDI because patients with CDI shed more *C. difficile* in their stool, with resulting increased skin and environmental contamination, and contamination of healthcare workers' hands, compared

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with asymptomatic carriers [11–13]. However, asymptomatic carriers are known to be a source of *C. difficile* transmission [14]. The relative importance of asymptomatic carriage on *C. difficile* transmission in the hospital may have changed since those original studies on *C. difficile* transmission, as at that time it was not the standard of care to place all patients with CDI in contact precautions. Several recent studies support this notion. Lanzas et al demonstrated, using compartment-based modeling, that patients who develop CDI in the hospital were just as likely to have acquired *C. difficile* from an asymptomatic carrier as a patient with CDI [15]. Eyre et al were able to attribute no more than 19% of new cases of CDI to a known prior case of CDI by using whole-genome sequencing and epidemiological data [16]. Likewise Curry et al [24], using multilocus variable number of tandem repeats analysis, found that 30% of new CDI cases were related to other, known CDI cases, and 29% of new CDI cases were related to other, known asymptomatic *C. difficile* carriers. Because of concerns that a large proportion of new CDI cases are a result of transmission from asymptomatic carriers, the objectives of this prospective epidemiological study were to determine the prevalence and risk factors for asymptomatic *C. difficile* carriage on admission to the hospital, and to compare *C. difficile* isolates present on admission in asymptomatic carriers to isolates from patients with CDI.

METHODS

Setting and Participants

This study was conducted at Barnes-Jewish Hospital. Patients were prospectively enrolled from June 2010 through October 2011. All newly admitted patients aged ≥18 years with an anticipated length of stay >48 hours to general medical and surgical services were eligible. Patients with diarrhea on admission were excluded. Data were collected on patients who were able to provide a stool specimen or rectal swab within 48 hours of admission. All references to *C. difficile* colonization refer to asymptomatic carriage, and all references to CDI indicate symptomatic infection (defined as diarrhea plus stool positive for *C. difficile* toxin). The Washington University Human Research Protection Office approved this project.

Data Collection

Patients were interviewed and medical records were reviewed. Demographic data, comorbidities, where the patient was admitted from, the service the patient was admitted to, the primary reason for admission, medications prescribed on admission, and stool frequency and consistency were recorded. Data were also collected on antimicrobial and healthcare exposures in the previous 90 days based on patient report and review of medical records. Inpatient exposures were defined as residing in a healthcare facility for at least 24 hours. Patients were monitored while hospitalized and contacted 60 days after discharge to determine if the patients were diagnosed with CDI.

Specimen Collection and Microbiological Examination

The first bowel movement of enrolled patients was collected. If the patient did not have a bowel movement within 48 hours of admission, a rectal swab was obtained (BD ESwab, Becton, Dickinson, and Company, Sparks, Maryland). Specimens were stored at −30°C until cultured. Specimens were cultured as previously described, using a method with reliable detection of as few as 10 colony-forming units of *C. difficile* per gram of stool [17]. In brief, 1 g of stool, or swab transport media, was heat-shocked at 80°C for 10 minutes. The specimen was then placed into cycloserine, cefoxitin, mannitol broth with taurocholate and lysozyme (Anaerobe Systems, Morgan Hill, California) and incubated anaerobically at 35°C. When turbid, broth was streaked onto prereduced blood agar (Becton, Dickinson, and Company). Identification of *C. difficile* was based on colony morphology, Gram stain, and biochemical testing. *Clostridium difficile* isolates were then inoculated into brain-heart infusion broth (Anaerobe Systems), and culture supernatant was tested for the presence of glutamate dehydrogenase and toxins A and B (C,diff Quick Chek Complete, Techlab, Blacksburg, Virginia).

Polymerase chain reaction (PCR) ribotyping was performed on all *C. difficile* isolates as previously described [18]. The ribotyping banding patterns were analyzed using the DiversiLab Bacterial Barcodes software, and isolates were considered identical if the similarity index was ≥95%. All unique strains were compared with the Cardiff-ECDC collection of *C. difficile* strains, which consists of 30 unique ribotypes. Unique strains that did not match any of the strains from the Cardiff-ECDC collection were given a Washington University (WU) strain number. *Clostridium difficile* isolates from asymptomatic carriers were compared with isolates obtained from patients with CDI from stool specimens collected under 2 different protocols during 2010: protocol A and protocol B. For both protocols, specimens from patients with recurrent CDI were excluded [19]. All toxigenic isolates from asymptomatic carriers were evaluated for the presence of binary toxin using a multiplex PCR as previously described [20].

Statistical Methods

Continuous data were normally distributed and compared between groups using the *t* test. Pearson χ^2 test and Fisher exact test were used for the analysis of proportions. Statistical significance was reached with a 2-sided *P* value <.05. Bonferroni corrections were made for multiple comparisons. All analyses were performed using SPSS for Windows software package, version 19.0.

RESULTS

Two hundred fifty-nine patients were enrolled and had a stool or rectal swab specimen collected within 48 hours of admission. *Clostridium difficile* was not isolated from 204 patients (78.8%; 95% confidence interval [CI], 73.4%–83.3%), toxigenic *C. difficile* (TCD) was isolated from 40 (15.4%; 95% CI, 11.6%–20.3%), and nontoxigenic *C. difficile* (NTCD) was isolated from 15 (5.8%; 95% CI, 3.5%–9.3%). There were no differences between TCD carriers and uncolonized subjects with regard to age (mean, 56 vs 58 years; $P = .46$), the proportion of patients who were admitted to the medical service (82.5% vs 88.2%; $P = .32$) or admitted from another healthcare facility (32.5% vs 23.5%; $P = .23$), or reason for admission ($P = .45$) (Table 1). There were no differences in any of 12 comorbidities or past history of CDI in the 90 days prior to admission (2.5% vs 2.0%; $P = .82$). Two (1.0%) of the uncolonized patients and 1 of the TCD-colonized patients (2.5%) were subsequently diagnosed with CDI ($P = .43$).

Healthcare exposures were very common, with 85.3% of uncolonized and 90.0% of TCD carriers ($P = .43$) having at least 1 inpatient and/or outpatient healthcare exposure in the

Table 1. Patient Characteristics and Comorbidities[a]

Variable	Uncolonized (n = 204)	Toxigenic *C. difficile* (n = 40)	Nontoxigenic *C. difficile* (n = 15)
Age, y, mean (SD)	58 (14.4)	56 (16.3)	52 (16.1)
White race	130 (63.7%)	29 (72.5%)	13 (86.7%)
Female sex	96 (47.0%)	22 (55.0%)	9 (60.0%)
Type of service			
Medicine	180 (88.2%)	33 (82.5%)	13 (86.7%)
Surgery	24 (12.8%)	7 (17.5%)	2 (13.3%)
Admitted from			
Home	156 (76.5%)	27 (67.5%)	11 (73.3%)
Other healthcare facility	48 (23.5%)	13 (32.5%)	4 (26.7%)
Admission reason			
Infection	60 (29.4%)	10 (25.0%)	5 (33.3%)
Chronic condition	75 (36.8%)	17 (42.5%)	6 (40.0%)
Elective surgery	10 (4.9%)	0	1 (6.7%)
New medical/ surgical problem	59 (28.9%)	13 (32.5%)	3 (20.0%)
Comorbidities			
Diabetes mellitus	76 (37.3%)	12 (30.0%)	3 (20.0%)
Congestive heart failure	37 (18.1%)	9 (22.5%)	2 (13.3%)
Liver disease	18 (8.8%)	5 (12.5%)	4 (26.7%)
Chronic kidney disease	34 (16.7%)	9 (22.5%)	3 (20.0)%
Chronic lung disease	46 (22.5%)	12 (30.0%)	4 (26.7%)
HIV	4 (2.0%)	0	0
Solid organ transplant	14 (6.9%)	2 (5.0%)	3 (20.0%)
Stem cell transplant	1 (0.5%)	0	0
Solid malignancy	10 (4.9%)	4 (10.0%)	1 (6.7%)
Hematological malignancy	3 (1.5%)	1 (2.5%)	2 (13.3%)
Inflammatory bowel disease	4 (2.0%)	1 (2.5%)	0
History of CDI	4 (2.0%)	1 (2.5%)	0
Developed CDI while hospitalized or during follow-up period	2 (1.0%)	1 (2.5%)	0

Data are presented as No. (%) unless otherwise specified.

Abbreviations: *C. difficile*, *Clostridium difficile*; CDI, *Clostridium difficile* infection; HIV, human immunodeficiency virus; SD, standard deviation.

[a] There were no statistically significant differences between groups.

Table 2. Healthcare Exposures in the 90 Days Prior to Admission[a]

Exposure	Uncolonized (n = 204)	Toxigenic *C. difficile* (n = 40)	Nontoxigenic *C. difficile* (n = 15)
Any healthcare exposure	174 (85.3%)	36 (90.0%)	15 (100%)
Inpatient exposures			
Acute care hospital	102 (50.0%)	20 (50.0%)	11 (73.0%)
No. of admissions[b]			
1–2	73 (71.6%)	17 (85.0%)	8 (72.7%)
>2	29 (28.4%)	3 (15.0%)	3 (27.2%)
Days since last discharge[b]			
1–30	72 (71.6%)	12 (60.0%)	8 (72.7%)
31–90	30 (29.4%)	8 (40.0%)	3 (27.2%)
LTCF/rehab	13 (6.4%)	4 (10.0%)	1 (6.7%)
Surgery in last 90 days	21 (10.3%)	7 (17.5%)	0
Abdominal	8	1	
Thoracic	4	2	
Orthopedic	4	2	
Others	5	2	
Outpatient exposures			
Visit to outpatient clinic	158 (77.5%)	34 (85.0%)	14 (93.3%)
No. of outpatient visits[b]			
1–4 visits	116 (73.4%)	23 (67.6%)	9 (64.2%)
>4 visits	42 (26.6%)	11 (32.4%)	5 (35.7%)
Days since last visit[b]			
1–30	126 (80.3%)	26 (76.5%)	9 (64.2%)
31–90	31 (19.6%)	8 (23.5%)	5 (35.7%)
Outpatient rehab	8 (3.9%)	3 (7.5%)	1 (6.7%)
Hemodialysis	8 (3.9%)	4 (10.0%)	3 (20.0%)

Data are presented as No. (%).

Abbreviations: *C. difficile*, *Clostridium difficile*; LTCF, long-term-care facility.

[a] There were no statistically significant differences between groups.

[b] Among patients with at least 1 exposure.

90 days prior to admission (Table 2). The proportion of uncolonized and TCD carriers with at least 1 admission to an acute care facility was identical at 50%. Likewise, there were no differences in the number of admissions or days since last discharge from an acute care facility, or proportion of patients who had a long-term-care facility or inpatient rehab exposure. One hundred fifty-eight (77.5%) uncolonized patients and 34 (85.0%) TCD carriers had at least 1 visit to an outpatient clinic, with similar proportions with >4 visits and visits within 30 days of admission. There was a trend for more TCD carriers to receive outpatient hemodialysis (10.0%; $P = .1$) and for significantly more NTCD carriers to receive outpatient hemodialysis (20.0%; $P = .006$), compared with uncolonized patients (3.9%).

Exposure to medications that have been associated with CDI was also common. Of the 204 uncolonized patients, 114 (55.9%) were exposed to antimicrobials, compared with 22 (55.0%) of TCD carriers (Table 3). Across the different classes of antimicrobials, compared with uncolonized patients, TCD carriers were more likely to be exposed to a penicillin (11.8% vs 27.5%; $P = .009$) or a cephalosporin (20.6% vs 40.0%; $P = .008$). There were no differences between TCD and NTCD carriers and exposure to these antimicrobials; however, there was a significant difference between uncolonized patients and NTCD carriers only for penicillins (11.8% vs 33.3%; $P = .02$). Macrolide exposures were also more common among NTCD carriers compared with uncolonized patients (12% vs 33%; $P = .02$). There were no differences across the carrier states and exposure to proton pump inhibitors, H2 blockers, antidiarrheal medications, and laxatives.

Overall, the heterogeneity of *C. difficile* strains recovered was high. The 40 TCD isolates obtained from the asymptomatic carriers corresponded with 12 different strain types. There were 74 TCD isolates representing 23 different strains from protocol A and 49 TCD isolates from protocol B representing 21 different strains. Two strains were unique to the asymptomatic carriers (ie, those 2 strains were not isolated in protocol A or protocol B), 8 strains were unique to protocol A, and 7 strains were unique to protocol B. Five strains were common to all 3 protocols. PCR ribotype 014/020 was the most common strain among the asymptomatic carriers (35%; Table 4), the third most common strain from protocol A (9%, $P < .001$), and the third most common strain from protocol B (12%, $P = .01$). PCR ribotype 012 was the second most common strain among the asymptomatic carriers (10 [25%]), but uncommon in the other protocols (protocol A: 1%, $P < .001$; protocol B: 0%, $P < .001$). There was only 1 (3%) strain of PCR ribotype 027 among the asymptomatic carriers, but this was the most common strain in both protocol A (31%; $P < .001$) and protocol B (16%; $P = .03$). Only 2 isolates from the asymptomatic carriers had the genes for binary

Table 3. Medication Exposures in the 90 Days Prior to Hospital Admission

Antimicrobial	Uncolonized (n = 204)	Toxigenic *C. difficile* (n = 40)	Non-toxigenic *C. difficile* (n = 15)
Any antimicrobial	114 (55.9%)	22 (55.0%)	9 (60.0%)
Penicillins	24 (11.8%)	11 (27.5%)*	5 (33.3%)*
Carbapenems	10 (4.9%)	3 (7.5%)	1 (6.7%)
Cephalosporins	42 (20.6%)	16 (40.0%)*	4 (26.7%)
Fluoroquinolones	29 (14.2%)	6 (15.0%)	4 (26.7%)
Metronidazole	12 (5.9%)	6 (15.0%)	0
Clindamycin	8 (3.9%)	2 (5.0%)	0
Vancomycin, intravenous	41 (20.1%)	11 (27.5%)	4 (26.7%)
Vancomycin, oral	3 (1.5%)	1 (2.5%)	0
Doxycycline	7 (3.4%)	1 (2.5%)	0
Linezolid	7 (3.4%)	1 (2.5%)	0
Daptomycin	1 (0.5%)	0	0
Trimethoprim/ sulfamethoxazole	12 (5.9%)	4 (10.0%)	2 (13.3%)
Macrolides	24 (11.8%)	7 (17.5%)	5 (33.3%)*
Aminoglycosides	6 (2.9%)	2 (5.0%)	1 (6.7%)
Other antimicrobial	13 (6.4%)	0	1 (6.7%)
Gastric acid suppression	103 (50.5%)	24 (60.0%)	7 (46.7%)
Proton pump inhibitor	77 (37.7%)	15 (37.5%)	7 (46.7%)
H2 blocker	26 (12.7%)	9 (22.5)	0
Antidiarrheals	82 (40.2%)	17 (42.5%)	8 (53%)
Laxatives	58 (28.4%)	11 (27.5%)	6 (40.0%)
Chemotherapy	5 (2.5%)	2 (5%)	0

Data are presented as No. (%).

Abbreviation: *C. difficile*, *Clostridium difficile*.

* $P \leq .02$ compared with uncolonized patients.

Table 4. Five Most Common Toxigenic *Clostridium difficile* Strains From Asymptomatic Carriers, Protocol A, and Protocol B

Asymptomatic Carriers (n = 40)		Protocol A (n = 74)		Protocol B (n = 49)	
Strain[a]	No.	Strain[a]	No.	Strain[a]	No.
014/020*,***	14 (35%)	027	23 (31%)	027	8 (16%)
012*,**	10 (25%)	106/174	9 (12%)	WU42	8 (16%)
053*	4 (10%)	014/020	7 (9%)	014/020	6 (12%)
077	3 (8%)	002	7 (9%)	001	4 (8%)
027*,***	1 (3%)	005	4 (5%)	106/174	3 (6%)

[a] Strain name is the polymerase chain reaction ribotype. If the strain did not match to a ribotype, the Washington University (WU) strain number is provided. If unable to discriminate between different ribotypes, both ribotypes the strain matched to are provided.

* $P \leq .005$, asymptomatic carriers compared with protocol A.

** $P < .001$, asymptomatic carriers compared with protocol B.

*** $P \leq .03$, asymptomatic carriers compared with protocol B.

toxin, the 027 strain and WU42. WU42 was present in protocol A (1%) and was one of the most common isolates from protocol B (16%; Table 4).

DISCUSSION

Several recent studies suggest that many new hospital-onset cases of CDI are not attributable to transmission from other, known cases of CDI in the hospital [15, 16, 21–24]. A potential source of *C. difficile* in these cases may be asymptomatic carriers, as a source of transmission to other patients and/or subsequent proliferation and development of CDI in the asymptomatic carrier. This study was conducted to determine the prevalence of, and risk factors for, asymptomatic carriage of TCD on admission to the hospital, and to determine if strain prevalence on admission is similar to strain prevalence among patients with CDI. The prevalence of asymptomatic TCD colonization on admission to the hospital in this study, 15%, was relatively high. In addition, there were no clear risk factors for asymptomatic TCD colonization. Known pathogenic strains were isolated from the carriers on admission. However, the prevalence of strains was different from those found from patients diagnosed with CDI during a similar time period. These findings taken as a whole indicate that we are far from understanding the optimal methods for preventing CDI in hospitalized patients.

Asymptomatic carriage on admission to the hospital is well described, with a reported prevalence of 0.6%–13% [11, 14, 25–33]. Of note, in contrast to the present study, many prior studies did not differentiate between TCD and NTCD. The lower limit of the 95% CI of just the TCD prevalence, 11.6%, was higher than the prevalence of total *C. difficile* colonization in all but 1 of the prior studies [27]. Among the studies where it is possible to determine the proportion of isolates that were TCD, TCD represented 52%–90% of all isolates [25, 27, 28, 32], and the prevalence of patients colonized with TCD on admission was 4.4%–9.7% [25, 27–30, 32].

Another striking finding of this study was a lack of association between colonization and healthcare or antimicrobial exposures. Every prior study that has assessed risk factors for asymptomatic *C. difficile* carriage on admission to the hospital has found prior healthcare exposures and/or antimicrobial exposures to be associated with *C. difficile* colonization [11, 14, 27, 29, 30, 32]. The prevalence of *C. difficile* colonization among patients with recent inpatient healthcare exposures is typically at least double (7%–17%) the prevalence among patients without inpatient healthcare exposures (3%–7%; $P \leq .013$) [14, 29, 30, 32]. The prevalence of TCD carriage in this study among patients with a recent inpatient healthcare exposure was 19.6% compared with 12.7% among those without ($P = .135$).

One potential explanation for the high prevalence of *C. difficile* colonization and the lack of association between colonization and healthcare/antimicrobial exposures in this study may be the highly sensitive methods used to detect colonization in this study [17]. It is recognized that antimicrobial exposures enhance the likelihood of multidrug-resistant organism detection from stool [34, 35]. Highly sensitive methods to detect *C. difficile* may be more likely to detect very low levels of *C. difficile* in patients without recent antimicrobial exposures. Rather than use culture, Leekha et al used PCR to detect *C. difficile* carriage [29]. They reported the sensitivity of PCR to be 86% compared with toxigenic culture without broth enrichment among patients with CDI [36]. Because the PCR used in their study was less sensitive than culture for detecting *C. difficile* in patients with CDI, we suspect that the culture-based method used in this study was more sensitive. An alternate explanation for the high prevalence of colonization identified is exposure to *C. difficile* in the community may be higher in the St Louis region and/or increasing in general. Studies have found correlations between community-onset CDI and incidence of hospital-onset CDI, and the incidence of community-onset CDI may be higher than previously thought [37–40]. The association between community-onset CDI incidence and hospital-onset CDI incidence may be a reflection of a higher prevalence of asymptomatic *C. difficile* carriage in those communities. At this point, when studying the epidemiology of asymptomatic *C. difficile* carriers, it is important to use the most sensitive methods available to detect *C. difficile*. Patients with extremely low concentrations of *C. difficile* may pose a lower risk for transmission to other patients; however, the risk may not remain constant for the duration of the hospital course. Exposure to antimicrobials may allow *C. difficile* to overgrow with subsequent increase in shedding and environmental contamination. It is also possible that the asymptomatic carrier may go on to develop CDI.

The results of the strain typing analysis in this study were consistent with previous investigations in that there was tremendous diversity [11, 14, 25, 30, 32, 41]. Each collection of isolates had strains unique to that collection, and there were only 5 strains common to all 3 collections. Loo et al found the proportion of NAP1 among asymptomatic carriers to be only 13%, compared with 63% for patients who developed CDI ($P < .001$) [30]. This study also found significantly fewer 027 isolates among the asymptomatic carriers compared with the patients with CDI. This is also consistent with the findings of Didelot et al [21]. Although they found that only 19% of cases of hospital-onset CDI could be traced to a known case of CDI, 63% of hospital-onset CDI cases caused by an 027 strain could be traced back to another patient. Conversely, this study identified more 014/020 isolates colonizing patients on admission compared with those causing CDI. The high prevalence of the 014/020 strain on admission is notable, as this may be an emerging stain of *C. difficile* [42, 43].

There are some limitations to this study. Although 259 patients were enrolled and 15.4% of patients were found to carry TCD, the sample size was relatively small. This may account for a lack of association between TCD colonization and prior healthcare and antimicrobial exposures. However, no trends were identified that would suggest this to be the case. When correcting for multiple comparisons, the associations between penicillin and macrolide exposures colonization status are not statistically significant. Conversely, the differences in colonization status and type of antimicrobial exposure may be related to type 1 error from the small sample size. Studies from the United States and abroad indicate there are regional differences in *C. difficile* strain distribution and CDI incidence [1, 37, 38, 42–45]. The high prevalence of *C. difficile* colonization and distribution of strains identified may not be generalizable.

Asymptomatic *C. difficile* carriage is common, but it is unclear what to do with this information. Asymptomatic carriers may be a source of new CDI cases, either as a reservoir for *C. difficile* transmission or due to subsequent development of CDI. Asymptomatic *C. difficile* carriers shed *C. difficile* and contaminate their environment, potentially posing a risk for transmission [13, 24]. Although past studies have indicated that asymptomatic TCD carriers were at lower risk for CDI than noncarriers, not all studies had the same findings [11, 46]. In this study, 3 (1%) patients developed CDI, one of whom was colonized with TCD. A recent multicenter study found that of 1256 patients enrolled, 82 (6.5%) had asymptomatic *C. difficile* colonization [47]. Twenty patients subsequently developed CDI, 9 (45%) of whom were colonized on admission. Prevention of CDI from asymptomatic carriers would likely differ based on whether on they are a source of transmission or are at risk for developing CDI. Food is another potential source of *C. difficile*. However, an ongoing follow-up study we are conducting indicates that food contamination with *C. difficile* in the hospital is very uncommon at <1% (authors' unpublished data).

In summary, using highly sensitive methods to detect asymptomatic *C. difficile* colonization, this study found a carriage rate of TCD higher than previous publications. In addition, there were no clear risk factors for asymptomatic colonization, and strain prevalence in carriers was different from patients with CDI. Additional study is needed to determine the role that asymptomatic *C. difficile* carriers have on hospital-onset CDI, whether it is necessary to screen for colonization, how to optimally screen for colonization, and what to do once asymptomatic carriers are identified.

Notes

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Potential conflicts of interest. E. R. D. has been a consultant for Merck, Sanofi Pasteur, and Rebiotix, and has performed research for Sanofi Pasteur, Optimer/Cubist, Viropharma, Merck, and Rebiotix. C.-A. D. B. has performed research for bioMérieux, Cepheid, Accelerate Diagnostics, and T2 Biosystems. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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